

was diffused as either diffused concentric narrowing of tertiary branches or significant obstruction of three or more major epicardial vessels.

On page 19, delete the paragraph immediately below the subheading 6.1.4.1 HLA

TYPING and replace it with the following paragraph:

Serological typing of HLA-A and HLA-B loci was performed by standard microcytotoxicity techniques. HLA-DR typing was performed by both serologic analysis and DNA techniques using sequence-specific oligonucleotide primers and the polymerase chain reaction.

On page 21, delete the paragraph immediately below the subheading 6.1.6

STATISTICAL ANALYSES and replace it with the following paragraph:

Kaplan-Meier univariate statistics were used to evaluate the relationship between cumulative high-grade rejection frequency and onset of TCAD, with p values calculated by log rank statistics (Kaplan, et al., 1958, J. American Statistics Association 53:457-481). Multivariable analysis of risk factors for a high-grade rejection over the 90 days following a low-grade EMB was performed using the Generalized Estimation Equations approach (Liang, et al., 1986, Biometrika 73:13-22) which incorporates a logistic regression model for the binary outcome, correcting for the correlation among observations in the same individual. For this analysis, events (high-grade rejections) were defined as the biopsy result nearest to 90 days following a low-grade biopsy. Variables considered as potential associated risk factors for a subsequent high grade rejection at the time of the low-grade biopsy included ischemic time, donor/recipient age, sex, race, matching at HLA-A, B, or DR loci, anti-HLA antibodies, and LGA. For variables determined to be associated with high-grade rejection in this analysis, positive and negative predictive values were evaluated using 2x2 contingency tables, as well as

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by Kaplan-Meier actuarial life tables. All data were analyzed using SAS system software (SAS Institute Inc., Cary, NC).

On page 23, delete the first paragraph and replace it with the following paragraph:

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mismatched (odds ratio 2.42, $p < 0.0001$), Figure 2. In contrast, donor/recipient matching at an MHC class I locus (HLA-A or HLA-B) did not influence progression to high-grade rejection (39% with no matches vs 36% for those with one or more matches, odds ratio 1.16, $p = 0.35$). The results validated our overall approach of identifying risk factors for progression of EMB to high-grade rejection, and enabled stratification of fully DR-mismatched recipients into a category requiring further immunologic monitoring.

On page 24, delete the paragraph immediately below the 6.2.5 subheading and replace it with the following paragraph:

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The relationship between anti-HLA antibodies measured at the time of a low-grade biopsy and subsequent high-grade rejection was investigated. As shown in Table 3, the presence of circulating IgG antibodies against MHC class II molecules (IgG anti-II) were associated with progression to a high-grade rejection within 90 days in individuals with complete donor-recipient HLA-DR mismatches, but not in those with at least one HLA-DR match. Among fully DR-mismatched individuals, 66% of low-grade EMBs accompanied by IgG anti-MHC class II antibodies progressed to a high-grade rejection compared with 42% of those without these antibodies ($p < 0.01$, odds ratio 2.68). Although in the initial analysis IgG anti-class I antibodies were associated with progression to high-grade rejection (odds ratio 1.92), this association in fact reflected the concomitant presence of IgG anti-MHC class II antibodies and was no longer evident after exclusion of individuals with IgG anti-MHC class II antibodies (progression to high-grade rejection occurred in 31% of EMBs with IgG anti-MHC class I

antibodies vs 34% without IgG anti-MHC class I antibodies, $p = 0.42$, odds ratio 0.83). IgM

AS anti-HLA antibodies were noted with subsequent high-grade cellular rejections.

On page 39, please delete Table 4. and replace it with the following Table 4.:

Table 4. Multivariable equation describing the patient incremental factors

associated with 90-day progression from a low-grade biopsy to a high grade rejection during the first year post cardiac transplantations.

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	<u>Odds ratio</u>	<u>95% CI</u>	<u>p value</u>
positive LGA	4.34	1.73, 10.91	0.0018
positive IgG anti-II	2.22	1.00, 5.02	0.0561
full DR mismatch	1.89	0.85, 4.27	0.1211

On page 1, insert as the first sentence of the specification following the title the following paragraph:

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This application claims priority to PCT/US98/20887 filed October 2, 1998 which claims priority to provisional application 60/090,153 filed June 22, 1998 and provisional application 60/060,992 filed October 3, 1997.

IN THE CLAIMS:

Please amend Claim 1 as follows:

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1. (amended) A method for assessing the risk of transplantation rejection in a recipient host comprising the following steps:
 - (a) determining the HLA-DR of the recipient and the HLA-DR of a donor and determining if the recipient and donor are DR mismatched;
 - (b) assaying for the presence of activated T-lymphocytes in the recipient;